Remarks

Claims 79-93 were pending in the subject application. By this Amendment, applicants have canceled claims 79 and 80 and amended claims 81-83 and 89. Consequently, claims 81-93 are currently pending.

Sequence Compliance

On page 2 of the February 24, 2003 Office Action, the Examiner alleged that the subject application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 for the reason(s) set forth on the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. Specifically, the Notice states that the Statement in Accordance with 37 C.F.R. 1.821(f), filed March 18, 2002, did not include a statement of "no new matter" as required under 37 C.F.R. 1.821(g).

In response, applicants attach hereto a copy of the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures as **Exhibit A**. Applicants also attach a Statement in Accordance with 37 C.F.R. §1.821(g) as **Exhibit B**, stating that applicants' March 18, 2002 sequence disclosures contained no new matter. Accordingly, applicants respectfully request that the Examiner withdraw this objection.

Oath/Declaration

On page 3 of the February 24, 2003 Office Action, the Examiner objected to the oath or declaration as being defective because the priority claim to PCT/US99/10151 is improperly made under both 35 U.S.C. §119(a)-(d) and 35 U.S.C. §120. The Examiner

requested that applicants provide a substitute Declaration claiming priority to PCT/US99/10151 under 35 U.S.C. §120 only.

In response, applicants attach hereto as **Exhibit C** a substitute Declaration claiming priority to PCT/US99/10151 under 35 U.S.C. §365(c) only.

Form PTO-1449

Applicants filed an Information Disclosure Statement on April 2, 2002 in connection with the subject application. Upon reviewing their files, applicants' undersigned attorney noticed that on page sixteen (16) of the From PTO-1449 the Examiner crossed out and did not initial the citation to one (1) pending U.S. application. The Examiner wrote that the entry was not a U.S. Patent.

In response, applicants point out that 37 C.F.R. 1.98(a)(1) makes it clear that an information disclosure statement must include "a list of all patents, publications, applications, or other information submitted for consideration by the office" (emphasis added). In addition, applicants draw the Examiner's attention to M.P.E.P. 609, entitled "Information Disclosure Statement," Section III(A)(1) which states in part

> ...U.S. applications must be must be identified by the inventor, the eight digit application number (the two digit series code and the six digit serial number), and the filing date...A separate list is required so that it is easy to confirm that applicant intends to submit an information disclosure statement and because it provides a readily available checklist for the examiner to indicate which identified documents have been

considered...Use of either form PTO-1449...to list the documents is encouraged (emphasis added).

Accordingly, pursuant to 37 C.F.R. §1.98(a)(1) and to M.P.E.P. 609, pending U.S. applications are to be disclosed in Information Disclosure Statements and are to be considered by the Examiner. The Examiner should then "indicate which documents have been considered" on Form PTO-1449. Accordingly, applicants respectfully request that the Examiner initial the citation to the pending U.S. application indicating that it has been considered on the Form PTO-1449 attached hereto as **Exhibit D**.

Rejection Under 35 U.S.C. §112, First Paragraph - Claims 79, 80, 83 and 89-93

On pages 3-6 of the February 24, 2003 Office Action, the Examiner rejected claims 79, 80, 83 and 89-93 under 35 U.S.C. §112, first paragraph, alleging the specification does not enable any person skilled in the art to which it pertains to use the invention commensurate in scope with these claims. In particular, the Examiner alleged that while the specification is enabling for an isolated nucleic acid comprising nucleotides having a sequence which encodes a functional activator of G protein signaling (AGS) protein which comprises amino acids having a sequence which is at least 98% homologous to the sequence set forth in SEQ ID NO:2, it does not reasonably provide enablement for nucleic acid molecules encoding non-functional AGS proteins.

In response, applicants draw the Examiner's attention to page 2, line 24 to page 3, line 4 of the subject application, where the term Activator of G protein Signaling (AGS) is described.

As is apparent, a protein referred to as an "AGS protein" necessarily functions as a G protein signaling activator. A protein which does not activate G protein signaling is, thus, not included in the scope of the term AGS. Accordingly, applicants contend that the currently pending claims, when read in light of the specification, do not read on nucleotide sequences which encode a protein which comprises amino acids having a sequence which is at least 98% homologous to the sequence set forth in SEQ ID NO:2 but which does not function as an activator of G protein signaling. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejection Under 35 U.S.C. §102 - Claims 79-85 and 87-92

On pages 6-7 of the February 24, 2003 Office Action, the Examiner rejected claims 79-85 and 87-92 under 35 U.S.C. §102(e), alleging that the claims are anticipated by Yen, U.S. Patent No. 6,462,177, issued October 8, 2002 and filed March 31, 1998.

In response, without conceding the correctness of the Examiner's rejection, applicants attach hereto as **Exhibit E** a Declaration Under 37 C.F.R. §1.131 signed by the inventors named on the subject application, stating that the subject matter of the pending claims in the subject application was conceived of and embodiments within the scope of the claims were reduced to practice prior to March 31, 1998. Applicants note that the Yen patent does not claim a nucleic acid molecule comprising nucleotides having a sequence encoding the protein having the amino acid sequence shown in SEQ ID NO:2. Consequently, the filing of a Declaration Under 37 C.F.R.

§1.131 is proper. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $920.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this response. However, if any other fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Gary J. Gershik 8/25/03
John P. White Date
Reg. No. 28,678
Gary J. Gershik
Reg. No. 39,992

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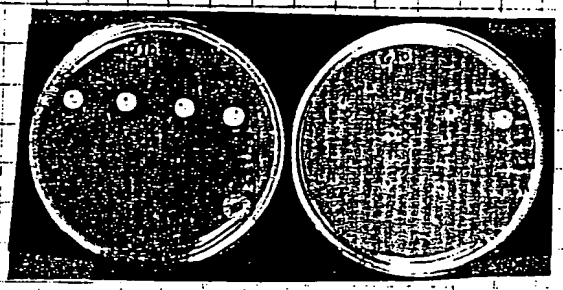
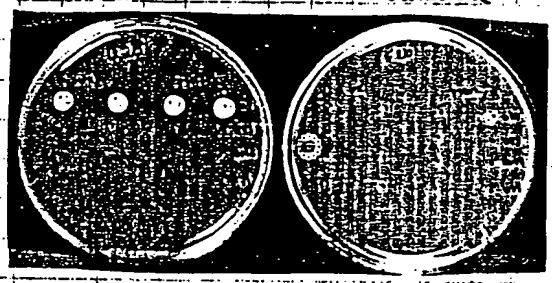
Project No._____

TEST OF UK W/ VARIOUS STRAINS + [AT]



10 mM AT

20 mM AT



Conclusions:

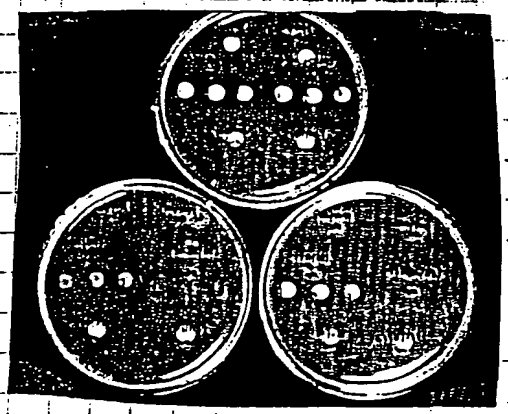
1. Gpa1(Q-HI)/Gai2 does not couple Gpr as well as Gpa1 or the Gpa1(Q-HI)/Gai2 G204A mutant (see Glucose 0 plates)

2. The presence of the UK insert confers growth on all Gα strains relative to pYES2. This growth is galactose dependent & presumably is due to expression of UK.

3. Expression of UK, however, seems to be inhibiting growth of 1316/1127 relative to pYES2. This was not seen before. Why?

4. Also, note that one of the two 1316/4098 isolates does exhibit lower growth than 1316/1183 when UK is induced. This may indicate an effect on Gα. May have to repeat this.

- Effect of STE5Δ:



SUCROSE-UT

GLUCOSE-UT+ 1mM AT

GAL-UT+ 1 mM AT

To Page No. 13

Witnessed & Understood by me,

Invented by Mary Cairns

Recorded by

Date

Project No._____

55 BOOK NO._____ TITLE CREATION OF POINT MUTANTS OF UK

TITL

From Page No.__

- UK looks like a ras-related G protein. It seems to have most of the conserved regions in small G proteins. Therefore, it may be possible to create "activating" & "inactivating" mutations of UK, as has been done with other small & heterotrimeric G proteins.

UK

MKLAAMIKKMCPSDSELSPAKINCYRMVILGSSKVGKTAIVSRFLTGRFEDAYTPTIEDFHRKFYSI
RGEVYQLDILDTSGNHPFPAMRRLSILTGDVFILVFSLDNRDSFEEVQRLRQQILMTKSCLENETKE
NVDVPLVICGNKCDADFYREVDQREIEQLVGDDPQRCAYFEISAKKNSSLDQHFRALFAMAKLPS
EMSPDLHRKVSVQYCDVLNKKALRNKKLLRAGSGGGGGDPGDAFGIVAPFARRPSVHSDLMYD
EKASAGSQAKDKERCVIS

P region - GTP hydrolysis. Consensus: GXXXXGK S/T

G' region - B-PO4 contact site. Consensus: DXXG

G region - Guanine ring contact. Consensus: NKXD

G" region - Guanine ring contact. Consensus (ras): ETSAK

Basic Region - thought to be important in anchoring to phospholipids in bilayer

CAAX Box - Lipid modification + anchoring methylation
X = S/T/A/C Farnesylation (ras)
X = Y/F/L/M/A Geranylgeranylation (rac)

- The ras G12V activating mutation is in sequence ...GAGGVGKSAL... in P region. UK does not have this G, but has 2 in the P region (at aas 31 & 36). These will be mutated to valine to see if one of them is an activating mutation.

- Glycine 81 in UK in the G' region is the equivalent of the G226 in Gas. Mutation of this to alanine should produce an inactive UK protein.

- Jeff designed the following mutagenic oligo pairs & performed the mutagenesis. He used the pcDNA3.1-His-UK plasmid as parent (UK can be excised with BamHI & EcoRI). Jeff confirmed mutations by sequencing & gave me back one isolate for each mutation.

G31 → V:

Analysis of "G-V1 FWD" a 31-mer DNA Oligonucleotide

5' CGC ATG GTC ATC CTC GTT TCG TCC AAG GTG G 3'

Oligonucleotide Analysis | Analysis Parameters

Analysis of "G-V1 REV" a 31-mer DNA Oligonucleotide

5' CCA CCT TGG ACG AAA CGA GGA TGA CCA TGC G 3'

Oligonucleotide Analysis | Analysis Parameters

To Page No. 97

Witnessed & Understood by me,

Invented by Mary Connell

Recorded by

Date

Witn